PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 April 2001 (03.04.01)	
International application No. PCT/EP00/06878	**Applicant's or agent's file reference** SPW99.04
International filing date (day/month/year) 17 July 2000 (17.07.00)	**Priority date** (day/month/year) 15 July 1999 (15.07.99)
Applicant DELEERSNIJDER, Willy et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

24 January 2001 (24.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Zakaria EL KHODARY
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10/030549

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
SPW99.04		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/06878	17/07/2000	15/07/1999
International Patent Classification (IPC) or national classification and IPC C07K14/72		
Applicant SOLVAY PHARMACEUTICALS B.V.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
VI	☐	Certain documents cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24/01/2001	24.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized officer De Kok, A Telephone No. +49 30 25901 314

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/06878

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-40 as originally filed

Claims, No.:

1-24 as received on 18/05/2001 with letter of 16/05/2001

Drawings, sheets:

1/3-3/3 as originally filed

Sequence listing part of the description, pages:

41-49, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☒ the claims, Nos.: 6
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 10, 16a, 16b, 17a, 17b, 18a, 20, 22, 23 second half sentence and 24 .

because:

   ☒ the said international application, or the said claims Nos. 16b, 17b, 17c, 18a, in relation to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 10, 16a, 17a, 20, 22, 23 second half sentence and 24.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9, 11-15, 16(b), 17(b)(c), 18, 19, 21 and 23, first half sentence
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-9, 11-15, 16(b), 17(b)(c), 18, 19, 21 and 23, first half sentence
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-9, 11-15, 18(b), 19, 21 and 23, first half sentence
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III:

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 16b, 17b,c and 18a relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V:

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. **Novelty and inventive step** (Article 33(2) and (3) PCT):

It appears from the examples that a cDNA encoding a putative G-protein coupled receptor (GPCR) has been obtained, but that the claimed polypeptides themselves have not been isolated. In other words, the putative biological activity/function of the protein encoded by the isolated cDNA has not been determined c.q. confirmed experimentally, thus said biological activity/function is purely speculative.

The only support for the function of the encoded protein, which is provided by the applicants is the sequence homology between the cDNA and the amino acid sequence derived thereof with some known GPCR's (see page 15, lines 1-16).

In conclusion, no proven or probable protein function is demonstrated in the application as filed.

However, additional experimental data provided by the applicant with respect to the identity of the natural ligand, justify the statement given in the specification that the IGS1 cDNA encodes a G-protein coupled receptor.

Since none of the documents cited in the International Search Report disclose a receptor having the claimed sequence and this natural ligand, novelty and inventive step can be acknowledged for claims 1-9, 11-15, 16b, 17b and c, 18, 19, 21 and claim 23 first half sentence.

2. **Industrial Applicability** (Article 33(4) PCT):

For the assessment of the present **claims 16b, 17b,c and 18a** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

1. Reference is made to the following document:

D1: MARTIN F ET AL.: MICROBIOLOGY, vol. 145, July 1999, pages 1605-1611

2. The abbreviation "IGS1" in the description and claims might be confusing as it stands also for intergenic spacer region (see document D1, abstract).

Re Item VIII

Certain observations on the international application

1. For claim 18 no working example has been given. Hence, for this claim the requirements of Article 5 PCT have not been fulfilled.

Claims

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
   a) a nucleotide sequence encoding the IGS1 polypeptide according to SEQ ID NO: 2;
   b) a nucleotide sequence encoding the polypeptide encoded by the DNA insert contained in the deposit no. CBS 102049 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands, in particular a nucleotide sequence corresponding to the SEQ ID NO: 1;
   c) a nucleotide sequence having at least 80 % (preferably at least 90%) sequence identity over its entire length to the nucleotide sequence of (a) or (b);
   d) a nucleotide sequence which is complimentary to the nucleotide sequence of (a) or (b) or (c).

2. The polynucleotide of claim 1 wherein said polynucleotide comprises the nucleotide sequence contained in SEQ ID NO:1 encoding the IGS1 polypeptide of SEQ ID NO:2.

3. The polynucleotide of claim 1 wherein said polynucleotide comprises a nucleotide sequence that is at least 80% identical to that of SEQ ID NO:1 over its entire length.

4. The polynucleotide of claim 3 which is the polynucleotide of SEQ ID NO:1.

5. The polynucleotide of claim 1-4 which is DNA or RNA.

6. A DNA or RNA molecule comprising an expression system, wherein said expression system is capable of producing an IGS1 polypeptide comprising an amino acid sequence, which has at least 80% identity with the polypeptide of SEQ ID NO:2 when said expression system is present in a compatible host cell.

7. A host cell comprising the expression system of claim 6.

8. A host cell according to claim 7 which is a yeast cell

9. A host cell according to claim 7 which is an animal cell

10. IGS1 receptor membrane preparation derived from a cell according to claim 7-9.

AMENDED SHEET
IPEA/EP

11. A process for producing an IGS1 polypeptide comprising culturing a host of claim 7 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture.

12. A process for producing a cell which produces an IGS1 polypeptide thereof comprising transforming or transfecting a cell with the expression system of claim 6 such that the cell, under appropriate culture conditions, is capable of producing an IGS1 polypeptide.

13. An IGS1 polypeptide comprising an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NO:2 over its entire length.

14. The polypeptide of claim 13 which comprises the amino acid sequence of SEQ ID NO:2.

15. An antibody immunospecific for the IGS1 polypeptide of claim 13.

16. A method for the treatment of a subject in need of enhanced activity or expression of IGS1 polypeptide receptor of claim 13 comprising:

(a) administering to the subject a therapeutically effective amount of an agonist to said receptor; and/or

(b) providing to the subject an isolated polynucleotide comprising a nucleotide sequence that has at least 80% identity to a nucleotide sequence encoding the IGS1 polypeptide of SEQ ID NO:2 over its entire length; or a nucleotide sequence complementary to said nucleotide sequence in a form so as to effect production of said receptor activity in vivo.

17. A method for the treatment of a subject having need to inhibit activity or expression of IGS1 polypeptide receptor of claim 13 comprising:

(a) administering to the subject a therapeutically effective amount of an antagonist to said receptor; and/or

(b) administering to the subject a polynucleotide that inhibits the expression of the nucleotide sequence encoding said receptor; and/or

(c) administering to the subject a therapeutically effective amount of a polypeptide that competes with said receptor for its ligand.

18. A process for diagnosing a disease or a susceptibility to a disease in a subject related to expression or activity of the IGS1 polypeptide of claim 13 in a subject comprising:

(a) determining the presence or absence of a mutation in the nucleotide sequence encoding said IGS1 polypeptide in the genome of said subject; and/or

(b) analyzing for the presence or amount of the IGS1 polypeptide expression in a sample derived from said subject.

19. A method for identifying agonists to the IGS1 polypeptide of claim 13 comprising:
(a) contacting a cell which produces a IGS1 polypeptide with a test compound; and
(b) determining whether the test compound effects a signal generated by activation of the IGS1 polypeptide.

20. An agonist identified by the method of claim 19.

21. The method for identifying antagonists to the IGS1 polypeptide of claim 13 comprising:
(a) contacting a cell which produces a IGS1 polypeptide with an agonist; and
(b) determining whether the signal generated by said agonist is diminished in the presence of a candidate compound.

22. An antagonist identified by the method of claim 21.

23. A recombinant host cell produced by a method of claim 12 or a membrane thereof expressing an IGS1 polypeptide.

24. A method of creating a genetically modified non-human animal comprising the steps of
a) ligating the coding portion of a polynucleotide consisting essentially of a nucleic acid sequence encoding a protein having the amino acid sequence SEQ ID NO: 2 or a biologically active fragment thereof to a regulatory sequence which is capable of driving high level gene expression or expression in a cell type in which the gene is not normally expressed in said animal; or
b) engineering the coding portion of a polynucleotide consisting essentially of a nucleic acid sequence encoding a protein having the amino acid sequence SEQ ID NO: 2 or a biologically active fragment thereof and reintroducing said sequence in the genome of said animal in such a way that the endogenous gene alleles encoding a protein having the amino acid sequence SEQ ID NO: 2 or a biologically active fragment are fully or partially inactivated.